

WHAT IS CLAIMED IS:

- 1 1. An isolated nucleic acid encoding an ABCG8 polypeptide, said
2 polypeptide comprising an amino acid sequence that is at least about 70% identical to an
3 amino acid sequence as set forth in SEQ ID NO:4 or 8.
- 1 2. The nucleic acid of claim 1, wherein said polypeptide specifically
2 binds to polyclonal antibodies generated against a polypeptide that comprises an amino
3 acid sequence selected from the group consisting of SEQ ID NO:4 and SEQ ID NO:8.
- 1 3. The nucleic acid of claim 1, wherein said polypeptide comprises an
2 amino acid sequence selected from the group consisting of SEQ ID NO:4 and SEQ ID
3 NO:8.
- 1 4. The nucleic acid of claim 1, wherein said polypeptide forms a
2 dimer with a second ABC polypeptide, and wherein said dimer exhibits sterol transport
3 activity.
- 1 5. The nucleic acid of claim 4, wherein said dimer is a heterodimer.
- 1 6. The nucleic acid of claim 4, wherein said sterol is cholesterol.
- 1 7. The nucleic acid of claim 5, wherein said second ABC polypeptide
2 is an ABCG5 polypeptide.
- 1 8. The nucleic acid of claim 7, wherein said ABCG5 polypeptide
2 comprises an amino acid sequence that is at least about 70% identical to an amino acid
3 sequence as set forth in SEQ ID NO:2 or 6.
- 1 9. The nucleic acid of claim 7, wherein said ABCG5 polypeptide
2 selectively binds to polyclonal antibodies generated against a polypeptide comprising an
3 amino acid sequence as set forth in SEQ ID NO:2 or 6.
- 1 10. The nucleic acid of claim 7, wherein said ABCG5 polypeptide
2 comprises an amino acid sequence selected from the group consisting of SEQ ID NO:2
3 and SEQ ID NO:6.

- 1 11. The nucleic acid of claim 7, wherein said ABCG5 polypeptide is
2 encoded by a nucleic acid that hybridizes under moderately stringent conditions to a
3 nucleic acid comprising a nucleotide sequence as set forth in SEQ ID NO:1 or 5.
- 1 12. The nucleic acid of claim 7, wherein said ABCG5 polypeptide is
2 encoded by a nucleic acid that comprises a nucleotide sequence that is at least about 70%
3 identical to a sequence as set forth in SEQ ID NO:1 or 5.
- 1 13. The nucleic acid of claim 1, wherein said nucleic acid hybridizes
2 under moderately stringent hybridization conditions to a nucleic acid comprising a
3 nucleotide sequence as set forth in SEQ ID NO:3 or 7.
- 1 14. The nucleic acid of claim 13, wherein said nucleic acid hybridizes
2 under stringent hybridization conditions to a nucleic acid comprising a nucleotide
3 sequence as set forth in SEQ ID NO:3 or 7.
- 1 15. The nucleic acid of claim 1, wherein said nucleic acid comprises a
2 nucleotide sequence at least about 70% identical to a sequence as set forth in SEQ ID
3 NO:3 or 7.
- 1 16. The nucleic acid of claim 1, wherein said nucleic acid comprises a
2 nucleotide sequence as set forth in SEQ ID NO:3 or 7.
- 1 17. The nucleic acid of claim 1, wherein said nucleic acid is from a
2 mouse or a human.
- 1 18. The nucleic acid of claim 1, wherein said nucleic acid is expressed
2 in the intestine or in the liver in the presence of an LXR agonist.
- 1 19. The nucleic acid of claim 1, wherein said nucleic acid is expressed
2 in a tissue selected from the group consisting of liver, jejunum, ileum, and duodenum.
- 1 20. An expression cassette comprising the nucleic acid of claim 1
2 operably linked to a promoter.
- 1 21. An isolated cell comprising the expression cassette of claim 20.

42. The method of claim 38, wherein said polypeptide is bound to a heterologous ABC polypeptide, forming a heterodimer.

43. The method of claim 38, wherein said functional effect comprises an increase in the sterol transport activity of said polypeptide.

44. The method of claim 38, wherein said functional effect comprises a physical interaction between said test agent and said polypeptide.

45. The method of claim 44, wherein said physical interaction is detected using a direct binding assay.

46. The method of claim 38, wherein said sterol-related disorder is sitosterolemia.

47. The method of claim 38, wherein said sterol-related disorder is selected from the group consisting of hypercholesterolemia, hyperlipidemia, gall stones, HDL deficiency, atherosclerosis, and nutritional deficiencies.

48. A method of identifying a compound useful in the treatment or prevention of a sterol-related disorder, said method comprising contacting a cell that expresses or is capable of expressing an ABCG8 polypeptide with a test agent, and determining the functional effect of said test agent upon said cell;
wherein a functional effect exerted on said cell by said test agent indicates that said test agent is a compound useful in the treatment or prevention of said sterol-related disorder.

49. The method of claim 48, wherein said sterol is cholesterol.

50. The method of claim 48, wherein said ABCG8 polypeptide comprises an amino acid sequence that is at least about 70% identical to an amino acid sequence as set forth in SEQ ID NO:4 or 8.

51. The method of claim 48, wherein said compound produces an increase in the expression of an ABCG8 gene that encodes said ABCG8 polypeptide.

1 52. The method of claim 51, wherein said increase in the expression of
2 said ABCG8 gene is detected by detecting the level of ABCG8 mRNA in said cell.

1 53. The method of claim 51, wherein said increase in the expression of
2 said ABCG8 gene is detected by detecting the level of ABCG8 polypeptide in said cell.

1 54. The method of claim 51, wherein said increase in the expression of
2 said ABCG8 gene is detected by detecting the level of ABCG8 protein activity in said
3 cell.

1 55. The method of claim 48, wherein said compound modulates the
2 level of sterol transport activity in said cell.

1 56. The method of claim 55, wherein said sterol transport activity in
2 said cell is detected by detecting the rate of sterol efflux in said cell.

1 57. The method of claim 56, wherein said sterol is cholesterol.

1 58. The method of claim 51, wherein said increase in the expression of
2 said ABCG8 gene is mediated by LXR or RXR.

1 59. The method of claim 48, wherein said sterol-related disorder is
2 sitosterolemia.

1 60. The method of claim 48, wherein said sterol-related disorder is
2 selected from the group consisting of hypercholesterolemia, hyperlipidemia, gall stones,
3 HDL deficiency, atherosclerosis, and nutritional deficiencies.

1 61. A method of treating or preventing a sterol-related disorder in a
2 mammal, said method comprising administering to said mammal a compound that
3 increases the level of expression or activity of an ABCG8 polypeptide in a plurality of
4 cells of said mammal.

1 62. The method of claim 61, wherein said sterol is cholesterol.

1 63. The method of claim 61, wherein said sterol-related disorder is
2 sitosterolemia.

64. The method of claim 61, wherein said sterol-related disorder is selected from the group consisting of hypercholesterolemia, hyperlipidemia, gall stones, HDL deficiency, atherosclerosis, and nutritional deficiencies.

65. The method of claim 61, wherein said compound produces a decrease in the amount of dietary sterol that is absorbed in said mammal.

66. The method of claim 61, wherein said compound produces a decrease in the amount of sterol that is retained in the liver of said mammal.

67. The method of claim 61, wherein said compound is identified using the method of claim 38 or 48.

68. The method of claim 61, wherein said compound causes an increase in LXR or RXR activity within cells of said mammal.

69. A method of prescreening to identify a candidate therapeutic agent that modulates ABCG8 activity in a mammal, the method comprising:
providing a cell which comprises an ABCG8 polypeptide; and
a test compound; and
determining whether the amount of sterol transport activity in said cell is increased or decreased in the presence of the test compound relative to the activity in the absence of the test compound;

wherein a test compound that causes an increase or decrease in the amount of sterol transport activity is a candidate therapeutic agent for modulation of ABCG8 activity in a mammal.

70. The method of claim 69, further comprising a secondary step, wherein said test compound is administered to a mammal, and the absorption of dietary sterol in said mammal is detected.